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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,310	03/14/2001	Samir Khleif	15280415100	9099

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
05/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/810,310	KHLEIF ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-8,11,12 and 14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6-8, 11, 12, 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed 3/15/07 is acknowledged and has been entered.

Claims 1, 2, 6-8, 11, 12 and 14-17 are presently being examined.

The following grounds of rejection remain.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 2, 6, 11, 12 and 14-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Corr *et al* (J. Exp. Med. 1996, 184: 1555-1560) in view of Corr *et al* (J. Immunol. 1997, 159: 49999-5004).

Corr *et al* (1996) teach IM injection of a viral protein antigen mixed with naked plasmid DNA encoding B7.1 or B7.2 co-stimulatory molecule. Corr *et al* (1996) teach that muscle cells at the site of injection do not present antigen to the immune system, but rather professional bone marrow-derived APCs present the antigen that results in a CTL response to said antigen.

Corr *et al* (1996) do not teach wherein the protein antigen comprising one or more T cell epitopes is administered separately from the said plasmid DNA encoding B7.1 or B7.2 co-stimulatory molecule to closely adjacent sites.

Corr *et al* (1997) teach that co-expression of B7-1 in the vicinity of a minimal MHC class I-restricted antigen is sufficient to prime a CTL response. Corr *et al* (1997) further teach IM or intradermal injection of protein antigen mixed with plasmid DNA encoding B7.1 or B7.2 co-stimulatory molecule. Corr *et al* (1997) teach that expression of the MHC class I restricted epitope in the same cell as the costimulatory ligand is not imperative for T cell priming, but *in vivo* a T cell cannot be effectively primed with a cognate signal from a peripheral somatic tissue if a second signal stimulus is not available in the immediate vicinity, for example in the same muscle. Corr *et al* (1997) teach that *in vivo* transfection of peripheral somatic tissues with plasmids encoding costimulatory ligands not only enhanced immune responses to antigen expressed by gene vaccination, but also dramatically increased the immune response to coinjected protein antigens. Corr *et al* (1997) teach that by increasing the density of membrane-bound costimulatory molecules, naked plasmid DNA injection can boost immune responses to soluble protein antigen in a manner analogous to conventional adjuvants, but without apparent systemic side effects. Corr *et al* (1997) teach that the plasmid DNA were constructed

with a promoter regulatory element for high expression (especially page 5001 at column 2, page 5001 at columns 1 and 2, page 5003).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the viral protein antigen taught by Corr *et al* (1996) or the CTL peptide epitope taught by Corr *et al* (1997) separately from the naked plasmid DNA encoding B7.1 and/or B7.2 co-stimulatory molecule to closely adjacent sites as taught by Corr *et al* (1997).

One of ordinary skill in the art would have been motivated to do this because co-administration or separate administration to closely adjacent sites are equivalent methods, and for convenience and standardization between administrations, because the same naked plasmid DNA preparation administered separately to a closely adjacent site could be used for co-ordinate immunizations with different protein or peptide antigens, and because Corr *et al* (1997) teach that co-expression of B7-1 in the vicinity of a minimal MHC class I-restricted antigen is sufficient to prime a CTL response, including wherein the antigen is a protein antigen. Claim 14 is included in this rejection because the peptide antigen administered separately to a closely adjacent site is "administered to the subject in a sequential vaccination protocol."

Applicant's arguments, of record in Applicant's response filed 3/15/07 (on pages 4-7), have been fully considered but are not persuasive.

Briefly, Applicant argues that the references do not render the claims prima facie obvious because the references do not teach or suggest separate administration to closely adjacent sites, nor do they provide a sufficient motivation to achieve this limitation as recited in the claims: (1) that all claim limitations be taught or suggested by the prior art, (2) there is not sufficient motivation to combine references to achieve the claimed invention, and (3) Corr (1977) demonstrates an immune response only when protein antigen and B7-encoding DNA are co-administered as a mixture, and hindsight reasoning is being applied.

It is the Examiner's position that In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning and to Applicant's point (1), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). It is the Examiner's further position that although Corr exemplifies coadministration, Corr teaches that the second signal only be available in the immediate vicinity of the MHC class I restricted epitope, such as for example, in the same muscle, and that it is not imperative for T cell priming that expression of the MHC class I restricted epitope be in the same cell as the costimulatory ligand.

In response to Applicant's argument that there is no suggestion to combine the references, the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation is found both in Corr (1997) as well as in the knowledge generally available to one of ordinary skill in the art as enunciated supra.

4. Claims 7 and 8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Corr *et al* (J. Exp. Med. 1996, 184: 1555-1560) in view of Corr *et al* (J. Immunol. 1997, 159: 49999-5004) as applied to claims 1, 2, 6, 11, 12 and 14-17 above, and further in view of WO 99/45954 A1.

Corr *et al* (1996) and Corr *et al* (1997) have been discussed supra, hereafter referred to as "the combined references." The combined references do not teach wherein the viral antigen is from HBV, HCV, HSV or HPV.

WO 99/45954 A1 teaches that epitopes on antigens such as HBV, HCV, HPV and HSV are useful in pharmaceutical compositions for both therapeutic and diagnostic applications. WO 99/45954 A1 further teaches that the peptides bind to class I HLA molecules, i.e., are about 8-11 amino acid residues in length (especially paragraph spanning pages 2-3, first full paragraph on page 3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have utilized the epitopes or protein antigens taught by WO 99/45954 A1 in the method taught by the combined references.

One of ordinary skill in the art would have been motivated to do this because the combined references teach an improved method for generating an effective immune response, and WO 99/45954 A1 teaches that epitopes on antigens such as HBV, HCV, HPV and HSV are useful in pharmaceutical compositions for both therapeutic and diagnostic applications.

Applicant's arguments, of record in Applicant's response filed 3/15/07 (on pages 7-8), have been fully considered but are not persuasive.

The Examiner's comments on Applicant's arguments at item #3 of this Action apply herein.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 7, 2007

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